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EXAMINER	
LEYBOURNE, JAMES J	
ART UNIT	**PAPER NUMBER**
2881	

DATE MAILED: 10/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	10/004,800	LOBODA, ALEXANDER V.
	Examiner	Art Unit
	James J. Leybourne	2881

-- The MAILING DATE of this communication appears on the cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *38-40* is/are allowed.

6)☒ Claim(s) *1-6,8-19,21,23-25,29-35,42 and 43* is/are rejected.

7)☐ Claim(s) *7,20,22,26-28,36,37 and 41* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. According to the "Amendment" A, received 26 June 3003, claims 1, 29, 31 and 33 have been amended; and claims 41-43 have been added.

2. Applicants arguments made with respect to claims have been considered but are moot in view of the new grounds for rejection.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless:
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e).

4. Claims 1-4, 16, 29, 31, 33, 42 and 43, are rejected under 35 U.S.C. 102(e) as being anticipated by Clemmer (6326482) in view of Russ et al. (6417511).

Regarding claim 1 Clemmer discloses a hybrid ion mobility and time-of-flight mass spectrometer instrument that has all of the limitations of claim 1 except an ion focusing section for receiving ions from the ion mobility section (IMS), comprising an RF ion guide having and means for supplying an RF voltage to the RF guide.

The system disclosed by Clemmer (figure 4) comprises an ion source region **32** in communication with an ion mobility spectrometer **34**, which itself is in communication with a mass spectrometer **36**. The spectrometer further comprises: an inlet for ions **68** and a mobility section **40** (see figure 4). An axial DC field is formed using guard rings **50** (column 7, lines 35-40). A buffer gas supply **46** has a flow rate controlled by computer or manually [0060]. Preferably, ion optics **47** is positioned between openings **45** and **84** to focus ions exiting opening **45** into an ion acceleration region of TOFMS 36.

Regarding claims 1, 16, 29, 33, 42 and 43, Clemmer does not teach an ion focusing section including an rf ion guide with the ion mobility being one of upstream from and integral with the ion focusing section.

Russ et al. teach a ring pole ion guide apparatus (Fig. 4) that can be used in a mass spectrometer system to guide ions from an ion source to a mass spectrometer <u>or between mass spectrometer stages</u>, or to dissociate ions into daughter ions in an ion dissociation system. The apparatus comprises an RF ion guide to focus the ions. It would be obvious to one of ordinary skill in the art at

the time of the invention to modify the hybrid ion mobility and time-of-flight mass spectrometer of Clemmer to include a ring pole ion guide between the IMS and the mass spectrometer as taught by Russ because in addition to focusing the ions, it could also be used as a collision cell and this would increase the functional capabilities of the system as in claims 42 and 43.

Regarding claim 2, Clemmer teaches (column 7, lines 13-18) describes an ion mobility spectrometer (IMS) **34** that includes a drift tube **40** having a gas port **42** disposed adjacent to an ion exit end **44** of tube **40**, wherein port **42** is connected to a source of buffer gas **46**. Clemmer does not teach that the source of buffer gas is mounted in the IMS, but for applications requiring a portable IMS/MS it would be obvious to mount the gas supply.

Regarding claims 3, 4 and 31, Clemmer teaches (column 7, lines 35-40) the drift tube **40** includes a number of guard rings **50** (plurality of rings) distributed along its inner surface, wherein the guard rings 50 are interconnected by equivalent-valued resistors (not shown). The guard ring positioned most adjacent to ion source region **32** is connected to a voltage source **VS1** to establish a constant electric field along the axis.

5. Claims 5-6, 8-19, 21, 23-25, 29-30 and 32-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Clemmer in view of Russ et al. as applied to claim 1and in further view of Thomson (6111250) and in still further view of Smith (USPN 6107628).

Smith teaches that to assist in the transfer of ions and other charged particles at lower pressures, the use of DC electrical (electrostatic) fields,

generated by a variety of methods, for the manipulation of charged particles or to assist in the collection of charged particles, is well known in the art. He also teaches that time varying (electrodynamic) or radio frequency (RF) electric fields can be applied for focusing purposes. An example of such RF devices are RF multipole devices in which an even number of rods or "poles" are evenly spaced about a line that defines the central axis of the multipole device (column 2, lines 29-44).

In the abstract, Thompson teaches that in a mass spectrometer, typically a quadrupole, one of the rod sets is constructed to create an axial field, e.g. a DC axial field, thereon. The axial field can be created by tapering the rods, or arranging the rods at angles with respect to each other, or segmenting the rods, or by providing a segmented case around the rods, or by providing resistively coated or segmented auxiliary rods, or by providing a set of conductive metal bands spaced along each rod with a resistive coating between the bands, or by forming each rod as a tube with a resistive exterior coating and a conductive inner coating, or by other appropriate methods.

Regarding claims 5 and 6, Thomson discloses providing an axial field in a quadrupole by segmenting the rods (columns 7 line 65 – column 8, line17). FIGS. 14 and 15 show a quadrupole rod set **96** consisting of two pairs of parallel cylindrical rods **96A**, **96B** arranged in the usual fashion but divided longitudinally into six segments **96A-1** to **96A-6** and **96B-1** to **96B-6**. Each A section and each B section is supplied with a different DC voltage V1 to V6 via resistors R1 to R6. Thus, sections 96A-1, 96B-1 receive voltage V1, sections 96A-2, 96B-2 receive

voltage V2, etc. The separate potentials can be generated by separate DC power supplies for each section or by one power supply with a resistive divider network to supply each section.

It would be obvious to one of ordinary skill in the art at the time of the invention to include an ion focusing section comprising an RF ion guide having means for supplying an RF voltage to the RF as discussed under claim 1 and further, to use segmented rods for the quadrupole, as taught by Thompson, in order to provide an axial field to speed the passage of ions through the ion guide.

Regarding claim 8, as discussed above, Thompson lists several means for forming a DC field and a potential gradient along the axis. One means listed is a multipole rod set arranged around an axis of an RF ion guide, with the rods of the multipole rod set having inclined surfaces whereby a potential gradient can be formed. Choosing a rod set with inclined surfaces to form the potential gradient is a mater of design choice.

Regarding claim 9, Clemmer teaches, in accordance with known IMS techniques, the buffer gas within drift tube **40** may typically be set within the range of between approximately one and a few thousand Torr (column 8, lines 23-27). Operating an Ion Mobility Spectrometer at atmospheric pressure (760 Torr) is well known in the art.

Regarding claim 10,Clemmer teaches using a matrix assisted laser desorption ionization (MALDI) as an ion source for a MIS/MS (column 13, lines 40-43). Selection of the source depends on the application.

Regarding claim 11, as discussed above, Thompson lists several means for forming a DC field and a potential gradient along the axis and Smith teaches, time varying (electrodynamic) or radio frequency (RF) electric fields can be applied for focusing purposes. One with ordinary skill in the art would be motivated to use segmented rods to provide the DC drift field because they could also provide focusing of the ions, as taught by Thompson.

Regarding claims 13-15, 23, 24, 29, 30, and 32-35, Clemmer discloses a system (Figure 9) that comprises a quadrupole mass filter and a collision cell provided between the IMS and the final mass analysis section. He does not include a quadrupole in the collision cell. However, Thomson teaches that a quadrupole can be used in a collision cell for fragmentation of parent ions (abstract). As discussed above, he also teaches that a segmented rod set can be used to apply an axial gradient. It would be obvious to one of ordinary skill in the art to modify the system disclosed by Clemmer in figure 9 to include a segmented RF quadrupole rod set in the collision cell for the reasons cited for claim 11.

With regard to claim 16, if the spectrometer of Clemmer were modified to comprise an ion guide as discussed under claim 1 it would have all of the limitations necessary to implement the method of claim 16 except one, namely maintaining a pressure in the RF guide sufficient to focus the ions along the axis. Smith teaches that when a multipole is used to confine an ion beam it can lead to focus the beam due to collisional damping in the presence of a gas. Based on

this teaching, one would be motivated to supply a pressure in the RF guide sufficient to focus the beam as cited in claim 16.

Regarding claims 12 and 19, Clemmer teaches the use of a time-of-flight MS in a MIS/MS hybrid spectrometer (column 6, lines 66-67).

With regard to claim 21, selecting groups of ions from the IMS that together encompass all of the ions eluting from the ion mobility section within a desired range of mass-to-charge ratios would be obvious to one of ordinary skill in the art.

With regard to claim 25, using a gate to control the flow of ions is well known in the art.

Regarding claims 17-18, Clemmer teaches a method of analyzing ions comprising separating a bulk of ions in time as a function of ion mobility, and separating in time as a function of ion mass at least a number of the ions separated in time as a function of ion mobility that define a first range of ion mobility (column 4, lines 8-22). It is inherent that implementing this method requires adjusting parameters of at least one of the mass analyzer and the drift region.

Allowable Subject Matter

6. Claims 38-40 are allowed.

The following is an examiner's statement of reasons for allowance:

With respect to claim 38 the prior art fails to disclose or make obvious a method of sequentially analyzing packets of ions that have been separated by their ion mobility) and adjusting parameters of the mass analyzer to follow changes in properties of ions eluting from the drift region.

Claims 39 and 40 are allowable by virtue of their dependence on claim 38.

7. Claims 7,20, 22, 26-28, 36-37 and 41 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

With respect to claims 7, 26-28 and 41, the prior art fails to disclose or make obvious a method of storing ions that have been separated in a drift tube as a function of ion mobility comprising providing the a RF ion guide as a multipole rod set comprising a plurality of rod segments providing different DC potentials to axially spaced rod segments, and the method further comprising:

- receiving ions from the drift region and initially applying a uniform potential gradient along the rod set;
- (b) after ions are uniformly distributed along the length of the rod set according to their mobility, establishing a potential well structure to retain groups of ions in separate potential wells; and
- (c) releasing ions separately from each potential well for subsequent mass analysis.

With respect to claim 20, the prior art fails to disclose or make obvious a method for analyzing ions which includes establishing for each group of ions an approximate range of mass-to-charge ratios present in the group, and mass

analyzing the ions in a Time-of-Flight mass analyzer, and setting timing of the Time-of-Flight mass analyzer in dependence upon the range of mass-to-charge ratios present in each group, thereby to enhance the sensitivity of mass analysis in the Time-of-Flight mass analyzer.

With respect to claim 22, the prior art fails to disclose or make obvious a method which includes, passing ions from the drift region of an IMS into a multipole rod set, providing the RF ion guides and providing an RF signal to the multipole rod set, to cool and focus the ions along an axis of the rod set, wherein the method further comprises adjusting at least one of the frequency and the amplitude of the RF to follow variations in mass-to-charge ratios of ions eluting from the drift region.

With respect to claims 36, the prior art fails to disclose or make obvious a method which includes at least one of: varying the potential gradient along the drift region with respect to time, thereby to vary the rate at which ions elute from the drift region; and providing a non-linear potential gradient along the drift region, whereby the potential gradient at an end of the drift region promotes elution of ions at a desired rate.

With respect to claim 37, the prior art fails to disclose or make obvious a method comprising switching the precursor ions selected by the first mass analyzer to correspond to an ion peak eluting from the drift region, thereby to maximize utilization of ions from a sample and enable sequential analysis of a plurality of different precursor ions present in the sample.

8. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

1. Any inquiry concerning this communication or earlier communications from the examiner should be directed to James J. Leybourne whose telephone number is (703) 305-7067. The examiner can normally be reached on M-F 9:00 - 6:30. If attempts to reach the examiner by telephone are unsuccessful, the

examiner's supervisor, John R Lee can be reached on (703) 308-4116. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9318 for regular communications and (703) 872-9317 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0956.

JJL

September 9, 2003

JOHN R. LEE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 2800